Peutz-Jeghers Syndrome and Management Recommendations

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Peutz-Jeghers syndrome (PJS) is an autosomal dominant disease caused by germline mutation of the serine threonine kinase 11 and characterized by hamartomatous polyps in the gastrointestinal tract and mucocutaneous melanin pigmentation. Patients with PJS are at increased risk for common and unusual types of gastrointestinal and nongastrointestinal tumors. This review analyzes currently available literature and describes the clinical characteristics of PJS, assesses the risk of malignancy in this disorder, and delineates management and surveillance recommendations for affected individuals.

Clinical Manifestations

History

Peutz-Jeghers syndrome (PJS) first appeared in the literature in the case report of Connor[1] published in 1895. Dr Connor, a British physician, described identical twin sisters with oral and labial pigmentation. Interestingly, one of the sisters died of intestinal obstruction at age 20 years and the other of breast cancer at age 59 years.[2,3] However, the presence of intestinal polyposis in these patients was not described. These twins were then illustrated by British surgeon J. Hutchinson[4] in 1896 and were subsequently known as the "Hutchinson twins." In 1921 Dr Johannes Peutz,[5] chairman of medicine at Johannes de Deo Hospital (Westeinde Hospital) The Hague, reported a Dutch family with gastrointestinal polyposis and distinctive pigmentation of the skin and mucous membranes and highlighted the inherited nature of the syndrome. In 1949 the combination of intestinal polyposis and pigmentation of the skin and mucous membranes was established as a distinct entity in a publication by Jeghers et al.[3] In 1954 A. Bruwer[6] coined the eponym "Peutz-Jeghers syndrome" in the title of his article on this disorder.[7]

Clinical Features

PJS is an autosomal dominant disease characterized by mucocutaneous pigmentation and hamartomatous polyps in the gastrointestinal tract.

This diagnosis can be made in patients with hamartomatous polyp(s) with at least 2 of the following clinical criteria also present: labial melanin deposits, a family history of the syndrome, and small bowel polyposis.[8] The syndrome appears equally in males and females and is found in all racial groups. Estimates regarding the incidence of PJS range from 1/50,000[9] to 1/200,000 live births.[10]

Pigmentation

PJS is characterized on physical examination by mucocutaneous pigmentation, usually occurring in infancy and fading in late adolescence[11] (Figure 1). The melanotic pigmented macules are dark brown or blue-brown, 1–5 mm in size, and located on the vermilion border of the lips (94% of patients), the buccal mucosa (66%), hands (74%), and feet (62%).[12] Periorbital, perianal, and genital pigmentation has also been noted. Present in more than 95% of affected patients, the pigmented spots are caused by pigment-laden macrophages in the dermis.[9] In contrast to PJS pigmentation, freckles are never located on the buccal mucosa or profusely around the nostrils and mouth.

Although similar type and location of pigmentation can be seen in the benign condition Laugier-Hunziker syndrome, several distinctions exist. First, Laugier-Hunziker syndrome lesions are progressively acquired in young or middle-age adults, profusion of periorificial pigmentation is usually not seen, conjunctival pigmentation can be seen, and these patients can have longitudinal melanonychia of the digits.[13,14]

Another syndrome, isolated melanotic mucocutaneous pigmentation, involves circumscribed macular pigmentation of the lips histologically similar to PJS. These patients have no small bowel polyps or mutation of the serine threonine kinase (STK)11/LKB1 gene, as seen in PJS, but female patients appear to have an increased risk of breast and gynecologic cancers.[15]

Abbreviations used in this paper: CLs, confidence limits; CT, computed tomography; MRI, magnetic resonance imaging; PJS, Peutz-Jeghers syndrome; STK, serine threonine kinase.

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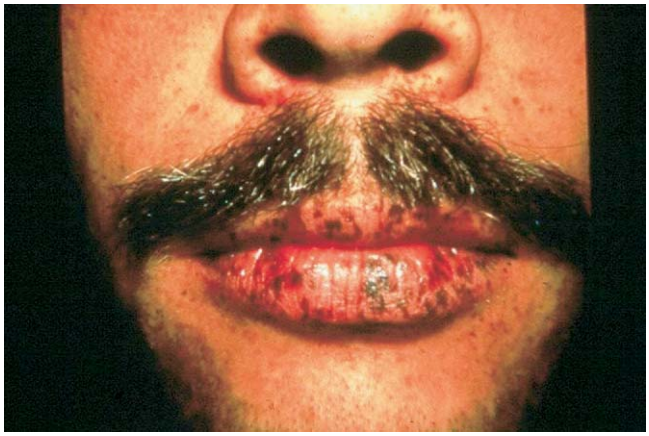

Figure 1. The classic labial melanin pigmented macules noted in PJS.

Hamartomatous Polyps

The Peutz-Jeghers polyp is a true hamartoma with unique histopathologic characteristics. These include the characteristic frond-like structure, appropriate epithelium for each area of the gastrointestinal tract, and associated smooth muscle proliferation (Figure 2). Histologically, Peutz-Jeghers polyps consist of a branching framework of connective tissue and smooth muscle lined by normal intestinal epithelium, rich in goblet cells. The polyps have elongated and convoluted glands and an arborizing pattern of growth.

In one study, polyps were detected in 88% of patients affected with PJS.[9] Peutz-Jeghers polyps occur most numerously in the small intestine but frequently in the colon and stomach.[16] The polyps usually number between 1–20 per segment of the intestinal tract and vary in size from 0.1–5 cm in diameter.[16] In affected individuals, polyps are seen at the following locations and frequency: small intestine (64%), colon (64%), stomach (49%), and rectum (32%).[9] They can also occur elsewhere with appropriate epithelium for that area,[17] and in case reports, they have been found in the renal pelvis, urinary bladder, lungs, and nares.[18,19]

Clinical Presentation

Peutz-Jeghers polyps grow during the first decade of life, and most patients become symptomatic between the ages of 10–30 years.[9] The average age of diagnosis of PJS is 23 years in men and 26 years in women. The presenting complaints of PJS are intestinal obstruction (43%), abdominal pain (23%), blood in the stool (14%), and anal extrusion of polyp (7%). The remaining 13% of cases are diagnosed because of melanin pigmentation. The most frequent complication in young age is intussusception, occurring in 47% of patients, primarily in the small intestine (in 95% of cases).

Genetic Defect

PJS is an autosomal dominant disorder with incomplete penetrance and variable expression that was initially linked to chromosome 19p13.3 in 1997.[20,21] In 1998, two separate laboratories described the cause of PJS as mutation in the STK11 gene, also known as the LKB1 gene.[22,23] STK11/LKB1 gene mutation is found in approximately 30%–70% of sporadic cases of PJS and 70% of affected individuals with a family history of the condition. The rate of spontaneous mutation in this disorder is unknown. The lack of identification of a STK11 gene mutation in all affected patients suggests the limitation of current molecular techniques, genetic mosaicism, or additional PJS loci.[24–27] With regard to the latter, some studies suggest linkage to loci on chromosome 19q and 16q.[28,29]

The STK11/LKB1 gene extends over 23 kb, is composed of 9 exons, and encodes a 433 amino acid STK protein.[22,23] Most mutations in PJS patients, including nonsense deletions, insertions, and rearrangements, lead to null alleles.[26] Of known STK11 mutations detected, about 65% affect the protein structure. However, missense mutations noted in the others are often of unclear clinical significance, leading to an inconclusive genetic testing result. Some evidence suggests that the STK11 gene is a tumor suppressor gene.[30] The serine/threonine kinase acts as a regulator of cell-cycle metabolism and cell polarity.[31] A genotype-phenotype correlation study

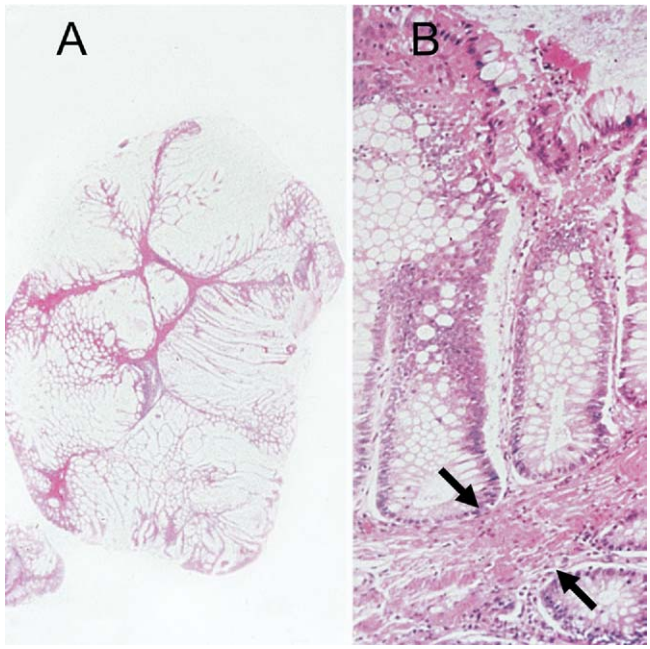

Figure 2. (*A*) Peutz-Jeghers polyp with branching framework of connective tissue on low power. (*B*) Smooth muscle (*between arrows*) lined by normal intestinal epithelium on high power.

noted that individuals with missense mutations had a significantly later time of onset to first polypectomy and other symptoms compared with individuals with truncating mutations or no detectable mutations.[27]

Currently, clinical genetic testing for mutations of the STK11 gene is available through several laboratories. The primary method used is sequencing of the entire coding area. The price of testing ranges from $975–$1400 for identification of the proband mutation with significant reduction of cost for evaluation of at-risk family members for a known pedigree mutation.

Cancer Risk

In 1975, Utsunomiya et al[9] described the natural history of PJS in Japan. These patients had a greater mortality rate than the general Japanese population but better survival than those with familial adenomatous polyposis. In 1987, Giardiello et al[8] first reported an increased risk of cancer in PJS. These investigators noted a history of gastrointestinal and nongastrointestinal cancers in 15 of 31 (48%) patients with PJS and calculated the relative risk of cancer in these individuals to be 18 times the general population risk. In 1989, this concept was supported by a review of patients from the St Mark's polyposis registry by Spigelman et al.[32] In this study 16 of 72 (22%) patients developed gastrointestinal and nongastrointestinal invasive malignancies. Hizawa et al[33] also described both gastrointestinal and nongastrointestinal cancers in Japanese PJS families.

Subsequently, a meta-analysis of cancer risk in 210 individuals described in 6 publications[8,32,34–37] showed that PJS patients have a relative risk for all cancers of 15.2 (95% confidence limits [CLs], 2.0, 19.0) and a lifetime risk of any cancer of 93%.[38] The gastrointestinal cancers at increased risk include cancer of the esophagus, stomach, small intestine, colon, and pancreas (Table 1). Of note, the lifetime risks for colon and pancreatic cancer are 39% and 36%, respectively. In addition, a high risk of nongastrointestinal cancers has also been noted (Table 1). These include cancer of the lung, breast, uterus, and ovaries.[38] Strikingly, the absolute risk for breast cancer in PJS is similar to the magnitude noted in hereditary forms of that tumor caused by germline mutations of BRCA1 and BRCA2 (genes associated with hereditary breast cancer). Analysis of case reports of malignancy in PJS not included in the meta-analysis reflected the spectrum of tumors and young age of diagnosis noted in the meta-analysis (Table 2).[38]

Other studies have highlighted the unusual types of associated tumors such as sex-cord tumor with annual tubules of the ovary and adenoma malignum of the cervix in female patients.[39] Also, testicular tumors of sex-cord and Sertoli-cell type have been associated with sexual precocity and gynecomastia in boys with this syndrome.[40]

Table 1. Absolute Rate and Cumulative Risk of Cancer in Patients With PJS from Ages 15–64 Years

Site	Rate per 100,000 person-years	Cumulative risk from age 15–64 y
All cancers	1304.6	93%
Esophagus	19.8	0.5%
Stomach	197.7	29%
Small intestine	118.6	13%
Colon	296.5	39%
Pancreas	118.6	36%
Lung	98.8	15%
Testes	39.2	9%
Breast	438.8	54%
Uterus	79.8	9%
Ovary	159.6	21%
Cervix	119.7	10%

Adapted and reprinted with permission from Giardiello FM et al.[38]

Further evaluation of cancer risk in PJS was reported by Lim et al.[41] Specifically, this study evaluated 240 individuals with known mutation of the STK11 gene. Overall, the risk of developing cancer by age 70 years was 81%. The most common cancers identified were gastrointestinal in origin (esophagus, stomach, small bowel, colorectum, pancreas). The cumulative risk for these cancers at age 60 years was 42%. The risk of breast cancer in women was substantially increased to 32% by age 60 years (Table 3).

Of note, the estimates of cancer risk by the above studies are limited by several considerations. In case reports of cancer in PJS families, preferential publication of pedigrees with high cancer rates can exaggerate risk. Also, in the major publications, ascertainment bias, which can also inflate risk estimates, is a concern for a rare disorder like PJS. Although the pedigrees in these studies appear not to have been recruited because of malignancy in the proband, bias cannot be eliminated. However, these factors are unlikely to account fully for the magnitude of cumulative risk noted in these publications.

Management

Screening of At-Risk Individuals

Most authorities recommend screening at-risk individuals (first-degree relatives of PJS patients) beginning at birth with annual history and physical examination with evaluation for melanotic spots, precocious puberty, and testicular tumors.[42] At-risk individuals who are asymptomatic and without stigmata at age 8 years should be offered

Table 2. Case Reports of Malignant and Nonmalignant Tumors in PJS

Site	No. of cases	Gender, M/F (% male)	Mean age of diagnosis ± standard deviation	95% Confidence limits	Age range (*y*)	Comments
Esophagus	1	1/0 (100)	67	—	—	
Stomach	8	5/3 (63)	30.1±16.7	16.1,44.1	10–61	
Small intestine	16	7/9 (44)	41.7±17.5	32.0,51.4	21–84	
Colorectal	9	7/2 (78)	45.8±17.3	32.4,59.0	27–71	
Pancreas	6	4/2 (67)	40.8±16.2	23.9,57.8	16–60	
Breast	0	0/9 (0)	37.0±11.4	28.2,45.8	19–48	3 cases bilateral
Cervix	28	0/28 (0)	34.3± 7.8	30.8,37.7	23–54	22 adenoma malignum
Ovarian	53	0/53 (0)	28.0±12.5	24.4,31.5	4–57	49/53 sex-cord tumors[a]
Testes	9	9/0 (100)	8.6± 5.4	4.3,12.7	3–20	All Sertoli cell

Adapted and reprinted with permission from Giardiello FM et al.[38]
[a]Concomitant breast cancer in 3 patients, breast cancer and cervical adenoma malignum in 3, breast and ovarian cancer in 1, cervical adenoma malignum in 10, ovarian adenocarinoma in 1, ovarian and cervical adenoma malignum in 5, Sertoli cell tumor in 3.

genetic testing for mutation of the STK11/LKB1 gene.[43,44] This young age of genetic screening can be justified by the benefit of avoiding the higher morbidity of emergent versus elective laparotomy for small bowel obstruction (as a result of intussusception), which occurs in about 30% of PJS patients by age 10 years.[45]

If genetic testing is performed and a mutation is found in an affected family member, then genetic testing of at-risk relatives will provide true positive or negative test results. At-risk members who receive true negative test results have a risk of PJS similar to that of the general population. At-risk relatives who test positive should follow the surveillance guidelines as described below.

If a mutation is not identified in the affected family member, testing at-risk relatives is inappropriate because the gene test will be inconclusive. Consequently, at-risk members are advised to pursue regular small intestinal contrast radiography every 2 years until 25 years old.[45] Other authorities suggest upper endoscopy, colonoscopy, and small bowel series at ages 12, 18, and 24 years.[42] Patients with melanotic pigmentation but uninformative genetic testing should follow surveillance guidelines.

Treatment

Most authorities recommend polypectomy for polyps in the stomach or colon that are greater than 1 cm in size noted during endoscopic surveillance.[16,44] Surgery has been recommended for symptomatic or rapidly growing small intestinal polyps or asymptomatic polyps greater than 1–1.5 cm in size.[10,16,43–46] Some experts suggest that an attempt to clear the small intestine of polyps ("clean sweep") should be made during laparotomy. This can be facilitated by concomitant interoperative endoscopy with polypectomy or, in the case of larger polyps, enterotomy. The clean sweep approach appears to decrease the need for recurrent small bowel surgery.[47] Recently, the use of double balloon enteroscopy for removal of small bowel PJS polyps has been reported and might decrease the need for laparotomy.

Surveillance of Affected Individuals

As noted above, individuals affected with PJS are at risk for a wide variety of cancers at a young age. Although no controlled studies on the effectiveness of cancer surveillance in PJS exist, a variety of recommendations derived from expert opinion are espoused in the literature. The risks of specific tumors in PJS are analyzed in concert with published expert opinion regarding cancer monitoring and surveillance recommendations. Table 4 lists the surveillance recommendation by organ and provides the published source(s). Table 5 orders these recommendations by age in a more clinically useful format.

Breast cancer. Of all tumors associated with PJS, breast cancer poses the greatest risk, affecting 32%–54%

Table 3. Cumulative Cancer Risk by Site and Age in STK11 Mutation Carriers

Type of cancer	20 y	30 y	40 y	50 y	60 y	70 y
All cancer	1% (0.3%, 4%)	3% (1%, 7%)	19% (12%, 28%)	32% (23%, 44%)	63% (49%, 78%)	81% (61%, 95%)
Gastrointestinal	—	1% (0.1%, 5%)	10% (5%, 18%)	18% (11%, 29%)	42% (26%, 61%)	66% (38%, 92%)
Breast	—	—	8% (3%, 23%)	11% (4%, 27%)	32% (15%, 59%)	—
Gynecologic	—	3% (0.7%, 11%)	6% (2%, 18%)	13% (5%, 31%)	13% (5%, 31%)	—
Lung	—	—	1% (0.1%, 6%)	2% (0.6%, 9%)	7% (2%, 25%)	7% (2%, 25%)

NOTE. 95% confidence limits in parentheses.
Adapted and reprinted with permission from Lim W et al.[41]

Table 4. Surveillance Recommendations

Cancer type	Age at initiation (*y*)	Surveillance	References
Breast[a]	18	Breast self-exam monthly	52–54
	25	Clinical breast exam semiannually	52–54
	25 (or earlier based on earliest age of onset in family)	Mammography annually (MRI offered as alternative)	52–54
Colon	18	Colonoscopy every 2–3 y	16,55,56
Pancreas	25–30	Endoscopic ultrasound every 1–2 y (CT scan and/or CA-19-9 offered as options)	42,58–60
Stomach and small intestine	8	Baseline upper endoscopy and small bowel series	45
	18	Upper endoscopy and small bowel series every 2–3 years	16,43–45,55,65
Ovaries	25	Transvaginal ultrasound and serum CA-125 annually	16,43,44,46,52,56,70
Uterus and cervix	21	Pelvic exam with Pap smear annually	72
	25	Transvaginal ultrasound and serum CA-125 annually	16,44,46
Testicles	Birth	History and physical exam with attention to examination of testicles and routine blood tests annually (ultrasound of the testicles every 2 y until age 12 offered as an option)	16,43

[a]Discuss option of prophylactic mastectomy on case by case basis and counsel regarding degree of protection and reconstruction options. The benefit of chemoprevention is unclear.

of PJS patients.[38,41] Review of meta-analysis and case reports showed a mean age of breast cancer diagnosis of 37 years, with a range of 19–48 years.[38] These risks are comparable to those for breast cancer in patients with hereditary breast and ovarian cancer caused by mutation of the BRCA1 and 2 genes (40%–85% lifetime risk of breast cancer).[48–51] Consequently, authorities recommend that PJS patients follow recommendations developed for BRCA1 and 2 mutation positive patients. These guidelines were originally developed by the Cancer Genetics Studies Consortium organized by the National Human Genome Research Institute[52] and were recently adopted by the National Comprehensive Cancer Network and modified by the American Society of Clinical Oncology.[53,54] The efficacy of these recommendations for cancer surveillance to reduce risk in individuals who carry predisposing mutations is unknown but is based on expert opinion concerning presumptive benefit.

The recommendations for women positive for a BRCA1 or BRCA2 mutation include monthly breast self-examination starting at age 18 years and semiannual clinical breast examination and annual mammography starting at age 25 years (initiation of mammography individualized on the basis of the earliest age of onset in the family). The substitution of magnetic resonance imaging (MRI) for mammography should be considered in women in whom mammography is technically limited. The option of prophylactic mastectomy might be discussed on a case by case basis, and counseling might be provided regarding the degree of protection and recon-

Table 5. Surveillance Recommendations by Age and Sex

Age (*y*)	Procedure for male patients	Procedure for female patients
From birth to 12	History and physical exam with attention to examination of testicles and routine blood tests annually (ultrasound of the testicles every 2 y until age 12 offered as an option)	History and physical exam with routine blood tests annually
At age 8	Upper endoscopy and small bowel series; if positive, continue every 2–3 y	Upper endoscopy and small bowel series; if positive, continue every 2–3 y
From age 18 on	Colonoscopy, upper endoscopy, and small bowel series every 2–3 y	Colonoscopy, upper endoscopy, and small bowel series every 2–3 years; breast self-exam monthly
From age 21 on	—	Pelvic exam with Pap smear annually
From age 25 on[a]	Endoscopic ultrasound every 1–2 y (CT scan and/or CA-19-9 offered as options)	Endoscopic ultrasound every 1–2 y (CT scan and/or CA-19-9 offered as options); clinical breast exam semiannually; mammography annually (MRI offered as alternative); transvaginal ultrasound and serum CA-125 annually

[a]Mammography might begin earlier on basis of earliest age of onset in family.

struction options. The benefit of chemoprevention is unclear. The similar magnitude of risk for breast cancer in PJS would argue for the adoption of these recommendations for women affected with PJS.

Colon. The lifetime risk of colorectal cancer in PJS patients is approximately 39%.[38] Therefore, most authorities recommend surveillance by colonoscopy but differ on the age of initiation.[16,43,44,55] Review of meta-analysis and case report data showed that the great majority of colorectal cancers occur after the age of 27 years, but these tumors have been reported during the teenage years.[38] Consequently, starting colonoscopic surveillance at age 18 years is recommended by several authorities, fulfilling the dictum of beginning surveillance 5–10 years before the earliest age of diagnosis of malignancy in the family. An interval of every 2–3 years is consistent with the increased frequency recommended for persons with comparable colorectal cancer risk as a result of family history.[56]

Pancreas. Pancreatic cancer is the third most common tumor affecting PJS patients with a lifetime risk of approximately 36%.[8,38] PJS is the strongest known risk factor for the development of pancreatic cancer, except for hereditary pancreatitis, which carries similar lifetime cancer risk (25%–40%).[57] A recent consensus conference of the International Hereditary Pancreatitis Study Group recommended screening these patients for pancreatic neoplasm.[58] Evidence from Brentnall et al[59] and Canto et al[60] suggests that early preinvasive pancreatic lesions can be detected in at-risk persons, including those with PJS, and treated before invasive cancer develops. Endoscopic ultrasound, helical computed tomography (CT), and MRI/magnetic resonance cholangiopancreatography are available for pancreatic cancer screening, but the efficacy of these tests is unclear. However, some data exist for endoscopic ultrasound,[60] which appears to be the best modality, with a low risk of adverse events and a high sensitivity for the detection of early pancreatic cancer.[61–64] In addition, endoscopic ultrasound–guided fine-needle aspiration can provide a histologic diagnosis of early cancer and detect dysplasia and precancerous lesions. The usefulness of CA19-9 as a screening test has not been established.

Review of meta-analysis and case report data showed that the average age of pancreatic cancer diagnosis is during the fifth decade of life, and the age range of diagnosis is between 16–60 years, with 95% of cases occurring after 24 years.[38] Consequently, starting pancreatic cancer surveillance on an annual or biennial basis at age 25–30 years is recommended by several authorities.[42,60]

Stomach and small intestine. The lifetime risk of gastric and small intestinal cancer is 29% and 13%, respectively. The average age of stomach cancer diagnosis was 30 years and of small intestine 42 years, as noted in meta-analysis and case reports. Cancers in both portions of the gastrointestinal tract have been found during the first and second decades of life.[38] Most authorities suggest surveillance of the stomach and small intestine with upper endoscopy and small bowel series every 2–3 years.[16,43–45,55] The use of capsule endoscopy to intermittently replace small bowel series and minimize radiation exposure has also been suggested.[65] Initiating surveillance at age 18 years is consistent with expert opinion. In addition, baseline upper endoscopy and small bowel series at age 8 years appear justified on the basis of case reports of early stomach and small intestinal cancer as noted above. Surveillance should continue every 2–3 years if polyps are noted at baseline evaluation.

Ovaries. Meta-analysis showed a 21% lifetime risk of ovarian cancer in patients with PJS, with most occurring during the fourth and fifth decades of life.[38] An increased risk for gynecologic cancers was also noted in STK11 gene mutation carriers.[41] Evaluation of case reports showed rare tumors of the ovaries including sex-cord tumors with annular tubules, cystadenomas, and granulosa cell tumors, with a mean age of diagnosis of 28 years (95% CLs, 24, 32).[38,66,67]

High risk of ovarian cancer was also seen in patients with BRCA1 or BRCA2 mutation (23%–54% lifetime risk) and those with hereditary nonpolyposis colorectal cancer (12% lifetime risk).[68,69] A consensus statement from the Cancer Genetics Study Consortium, derived from expert opinion, advocates transvaginal ultrasound with color Doppler and serum CA-125 level done annually or semiannually beginning at age 25–35 years for BRCA1 and BRCA2 mutation carriers.[52] Also, ovarian screening with transvaginal ultrasound and serum CA-125 is recommended by other consensus committees for patients at risk for hereditary nonpolyposis colorectal cancer.[56,70] In addition, PJS surveillance guidelines from other experts have recommended ovarian screening by ultrasound beginning at age 25 years.[16,43,44,46] Consequently, screening with annual transvaginal ultrasound and CA-125 beginning at age 25 years seems reasonable in patients with PJS on the basis of age of development of these tumors.

Uterus and cervix. The approximate lifetime risk of uterine and cervical cancer in PJS is 9% and 10%, respectively.[38] An increased risk for gynecologic cancers was also reported in STK11 gene mutation carriers.[41] Of note, a high percentage of cervical cancers in this syn-

drome are adenoma malignum, a rare well-differentiated cervical adenocarcinoma with a poor prognosis.[71] In case reports, the mean age at diagnosis was 34 years (95% CLs, 31, 38), with some patients diagnosed as young as age 23 years.[38] Screening by pelvic examination with Pap smear every year starting at age 21 years, as recommended for the general population, should include a high index of suspicion for adenoma malignum on Pap smear analysis.[72] In addition, transvaginal ultrasound with CA-125, starting at age 25 years, as recommended for ovarian cancer screening, appears appropriate.[16,44,46]

Testes. Review of the literature showed the development of testicular cancer at a mean age of 9 years (95% CLs, 4, 13) with a range of 3–20 years. All tumors were Sertoli cell tumors.[38] Expert opinion recommends annual history and physical examination, with attention to examination of the testicles, and routine blood tests. Ultrasound of the testicles every 2 years from birth to age 12 years has also been recommended.[16,43]

Conclusion

PJS, caused by germline mutation of the STK11 gene, is an autosomal dominant condition characterized by hamartomatous polyps primarily in the small intestine and mucocutaneous melanin pigmentation. With recent advances, screening at-risk individuals can now be done by genetic testing. The disorder is complicated in children and teenagers by small bowel intussusception. Moreover, adults are at high risk for development of gastrointestinal and nongastrointestinal cancer, which impacts on patient survival. Consequently, attention to age and gender-specific cancer surveillance is a vital aspect of managing patients with PJS (Table 5).

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